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Differences in risk behaviours and HIV status between primary amphetamines and opioid injectors in Estonia and Russia

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ABSTRACT

Background and objective

People who inject drugs (PWID) account for over half of new HIV infections in Eastern Europe and central Asia, where opioids continue to be the dominant illicit drugs injected. Stimulants including amphetamines (ATS) have been associated with HIV infection risk in several settings. We sought to examine whether primary ATS injection was associated with greater HIV risk, compared to opioid injection in two European locales with significant HIV epidemics.

Methods

PWID in Kohtla-Järve and St. Petersburg were recruited using respondent-driven sampling in 2012-2013. Survey data on demographic characteristics, service use, injecting and sexual risk behaviours; and HIV-status (and HCV in Kohtla-Järve) were compared between primary opioid and ATS injectors using logistic regression models.

Results

Of 591 injectors recruited in Kohtla-Järve and 811 in St. Petersburg, 195 (33%) and 27 (4%) primarily injected ATS in each city. In both cities, ATS injectors were younger than opioid injectors, initiated injection later, injected less frequently and were more likely to have been paid for sex. In both cities, PWID had high levels of multiple sex partners. In Kohtla-Järve, ATS-injectors had lower odds of back-loading and greater odds of polydrug use than opioid-injectors. In St. Petersburg, where over half of PWID reported unsafe sharing practices, ATS-injectors were less likely to report these practices. ATS-injection was negatively associated with being HIV positive in Kohtla-Järve (aOR=0.6; 95%CI: 0.5-0.8) and St. Petersburg (aOR=0.3; 95%CI: 0.1-0.7). ATS-injection was negatively associated with HCV-reactivity in Kohtla-Järve (aOR=0.5; 95%CI: 0.3-0.6).

Conclusions

In both locations, primary ATS injection was associated with lower injecting risk behaviours, lower odds of HIV and being paid for sex compared to opioid injection. Interventions targeting the characteristics and needs of ATS injectors are needed to increase contact with services and reduce sexual and injecting risk. Harm reduction services, including sexual risk reduction, need to be expanded for all PWID in St. Petersburg.

INTRODUCTION

People who inject drugs (PWID) were estimated to account for 51% of new human immunodeficiency virus (HIV-1) infections in Eastern Europe and central Asia in 2014, a region with the fastest growing HIV epidemic associated with injection drug use globally (UNAIDS, 2016; UNODC, 2016).

Opioid injection has been the main driver of HIV epidemics in Estonia and the Russian Federation, where over half of PWID in Kohtla-Järve (Estonia) and St. Petersburg (Russian Federation) were seropositive in 2012 (El-Bassel, et al., 2013; Jolley, et al., 2012; Uusküla, Raag, et al., 2015; Walsh, et al., 2013). Both cities are situated on the Baltic Sea, on the northern part of two major heroin trafficking corridors linking Afghanistan to the heroin markets of Western Europe; both have experienced HIV epidemics driven by transmission among PWID since the late 1990s (UNODC, 2012, 2015b). Despite similar HIV prevalence, estimated incidence was higher in Kohtla-Järve (22/100 person-years, 2012) than in St. Petersburg (7.2/100 person-years, 2010), partly due to the higher proportion of young PWID in the Estonian city and to differences in the context and epidemic response, presented in Table 1. Evidence-based harm reduction interventions, including needle and syringe programmes (NSP) and opiate substitution treatment (OST), were introduced in Kohtla-Järve in 2004 (Estonia Ministry of Health, 2014; Mathers, et al., 2010) whereas in St Petersburg, OST remains illegal and clean needles and syringes are not endorsed by government and provided by a few non-governmental organisations (Degenhardt, et al., 2014; EMCDDA, 2015).

Most PWID injected heroin and illicitly-produced synthetic opioids, namely fentanyls in Kohtla-Järve (introduced into Estonia following a heroin shortage in 2000) and methadone in St Petersburg (Eritsyan, et al., 2013; Heimer, et al., 2015). Estonia has reported one of the highest prevalences of amphetamine type stimulant (ATS) use in Europe (EMCDDA, et al., 2012; UNODC, 2014) and ATS have emerged as a major secondary drug among PWID in Kohtla-Järve and St. Petersburg (EMCDDA, 2010; Grund, et al., 2009; UNODC, 2015a).

ATS are psycho-stimulants that are relatively easy to synthesize and increasingly injected in settings previously dominated by opiates (Bao, et al., 2012; Booth, et al., 2008; Grund, et al., 2009). ATS have been associated with greater sexual risk, including multiple sex partners and unprotected sex, which may compound the risks of HIV acquisition among PWID (Baker, et al., 1994; Booth, et al., 2008; Darke, et al., 2008; Gleghorn, et al., 1998; Molitor, et al., 1999; Molitor, et al., 1998). ATS injection has also been associated with

more frequent injecting, needle/syringe sharing and HIV infection in settings where PWID also injected other drugs (Braine, et al., 2005; Hayashi, et al., 2011; Kozlov, et al., 2006; Tavitian-Exley, et al., 2017) but not when stimulants were reported as main injection drug (Booth, et al., 2008; Kral, et al., 1998; Swe, et al., 2012; Talu, et al., 2010). Few studies have examined drug use patterns by main drug injected and potential associations with risk behaviours and HIV and HCV infection in Eastern European settings (Booth, et al., 2008; Harrell, et al., 2012; Talu, et al., 2010; Tavitian-Exley, et al., 2015) and the relevance of ATS injection in shaping these epidemics remains unclear (EMCDDA, et al., 2011; EMCDDA, et al., 2014).

Our aim is to assess whether primarily injecting ATS as compared to opioids (heroin, synthetic heroin or methadone) is associated with increased injecting and sexual risk behaviours and HIV status among PWID in Kohtla-Järve (Estonia) and St. Petersburg (Russian Federation), two East European locales with significant and epidemiologically similar HIV epidemics.

METHODS

Study population

Integrated biological and behavioural surveys of HIV prevalence were conducted among PWID in Kohtla-Järve between May and July 2012, and in St. Petersburg from November 2012 to June 2013. These surveys used comparable recruitment criteria and respondent-driven sampling (RDS) survey methodology and have been reported on and described previously (Cepeda, et al., 2015; Dukhovlinova, et al., 2015; Heimer, et al., 2015; Tavitian-Exley, et al., 2017; Uusküla, Raag, et al., 2015). Briefly, RDS starts with a diverse sample of seeds (6 seeds in Kohtla-Järve and 12 seeds in different districts of St. Petersburg, subsequently increased to 16 to cover key districts and compensate for unproductive seeds). Seeds were selected through needle/syringe programmes (NSP) to represent a range of demographic and drug profiles; interviews and testing were conducted in fixed (Kohtla-Järve) and mobile clinics (St Petersburg). Each seed and subsequent participants were given an opportunity to recruit up to three PWID until a predetermined sample size was reached. Men and women aged 18 years or over, who had injected drugs in the past 30 days, lived in Kohtla-Järve or St. Petersburg and provided informed consent for the study were eligible. Eligibility was verified by the presence of injection marks and questions on injection practices before the start of the interview.

Measures

Information on demographic and social factors, injection and sexual risk behaviours and access to harm reduction services were recorded by trained fieldworkers in a structured confidential interviewer-administered questionnaire, using standardised study items and questions from established survey instruments (e.g. WHO Drug Injecting study Phase II survey v2b) (Des Jarlais, et al., 2006; Uusküla, Raag, et al., 2015).

HIV, HCV and HSV status

HIV sero-status was assessed using an HIV Antigen/Antibody Combo Assay (ADVIA Centaur, Siemens Healthcare Diagnostics) and HIV I/II Score line assay confirmatory test (INNO LIA, Fujirebio Europe) in Kohtla-Järve; rapid oral HIV testing was conducted in St. Petersburg using OraQuick ADVANCE® Rapid HIV-1/2 Antibody Tests (OraSure Technologies Inc.) and confirmed at the City AIDS Centre (Uusküla, Raag, et al., 2015). In Kohtla-Järve only, HCV and Herpes Simplex Virus (HSV) reactivity were measured using commercially available kits for antibodies to HCV (Murex anti-HCV v 4.0) and HSV-2 (HSV-2 IgG ELISA, IBL International GmbH).

The primary drug injected was categorised into mutually exclusive groups of primary ATS or primary opioid-injectors, based on the survey item *main drug injected in the past 4 weeks*. Injectors reporting no or "other" primary drug were compared with the rest of the sample and examined in descriptive analysis (and excluded in regression modelling).

Demographic and contextual variables

Demographic and contextual variables included age, sex, ethnicity, highest level of education completed (basic education/secondary and above), main source of income, living arrangements (stable/unstable), past month contact with an NSP, past year drug treatment (opioid substitution in Kohtla-Järve; any drug treatment in St. Petersburg) and having needles or syringes confiscated by the police.

Injecting and sexual risk behaviours

The behavioural variables examined included injecting-risk (using a 30 day recall period), sexual-risk behaviours (using a 6 month recall period) and serological markers for HIV (and in Kohtla-Järve only, HCV and HSV). Injecting behaviours of interest were past month injecting frequency (≥daily injecting vs. <daily injecting), intensity of injection on the last day injected (≥ 2 injections/day vs. <2 injections/day), injecting with used needles/syringes (sharing), sharing drug paraphernalia, back-loading (filling a syringe from a used syringe) and polydrug use (injecting a main drug and at least one other drug

in the last month). Sexual risk behaviours included having a sex partner (regular or casual) who injected drugs, having been paid for sex (i.e. receiving money or drugs for sex ever), multiple sex partners (≥ 2 sex partners in last 6 months) and consistent condom use (i.e. always) with sex partners. The variable "any sex in the last six months" was used to exclude non-sexually active PWID.

Statistical analyses

Descriptive statistics are presented for Kohtla-Järve and St. Petersburg separately (RDS-adjusted estimates, using the RDS-II estimator, are presented in supplementary material) (Volz, et al., 2008; Volz, et al., 2012; White, et al., 2015).

Two sets of logistic regressions were performed. The first set examined the determinants of ATS- and opioid-injection. In the second set, we assessed whether ATS was associated with a) injecting-risk behaviours, b) sexual-risk behaviours, and c) HIV, HCV and HSV prevalence. For both sets of regressions, we generated univariate and multivariable estimates (Kirkwood, et al., 2003; UCLA Statistical Consulting Group, 2015). Results for the multivariable regressions were adjusted for age, sex, education, living arrangements and duration of injecting. In the second set of regressions, we additionally adjusted for contact with NSP and drug treatment. These variables were judged to be important potential confounders, based on published evidence and our conceptual framework (Supplementary material: Figure S.1) (Lemstra, et al., 2012; Marshall, et al., 2008; Marshall, et al., 2011; Poundstone, et al., 2004; Tavitian-Exley, 2016). Variables were examined for collinearity and omitted from the model if their variance inflation factor (VIF) was > 2.5. A complete case analysis was used and observations with missing values were omitted. Odds ratios (OR) with 95% confidence intervals (95%CI) were calculated while also adjusting for clustering of observations by recruitment seed (Kirkwood, et al., 2003). Clusters were defined by a recruitment chain started by a given seed to account for the possibility that participants may be more likely to recruit other PWID with similar characteristics. This was achieved using the *svy* command in Stata (v.13.1) as in univariate analysis (Hosmer, 2000; Kirkwood, et al., 2003; StataCorp., 2013; UCLA Statistical Consulting Group, 2015). Sampling weights were not taken into account in the regressions as their use is often unwarranted for causal inference (Solon, et al., 2013).

Ethics

Ethical approval was obtained from the Ethics Review Board of the University of Tartu (Estonia), the Institutional Review Board at NGO Stellit in St. Petersburg (Russian Federation), and the Human Investigation Committee at Yale University (USA).

RESULTS

Characteristics of study sample

Our study included 591 PWID in Kohtla-Järve and 811 in St. Petersburg (Table 2; supplementary material Table S.1). In both cities, the majority of PWID were male, Russian-speaking or reporting stable living conditions (Table 2; Table S.1). However, more PWID in Kohtla-Järve were under the age of 30 and salaried or with a regular job than in St. Petersburg.

The primary drug commonly injected by PWID in both cities was a synthetic opioid (i.e. illicitly-manufactured fentanyl congeners in Kohtla-Järve, heroin and methadone produced in illicit laboratories in St. Petersburg) while ATS was the second most common drug class. Opioids were the primary drug for 61% of PWID in Kohtla-Järve and 96% in St. Petersburg; ATS was the main drug for 33% in Kohtla-Järve and 4% in St. Petersburg (6% of PWID in Kohtla-Järve had another or no primary drug).

More PWID had been in contact with a NSP in the past six months in Kohtla-Järve (82%) than in St. Petersburg (16%) and over half had ever received some form of attention for substance use disorder (Table 2). Substitution treatment was reported by 13% of PWID in Kohtla-Järve and detoxification by 11% in St. Petersburg in the past 12 months. Similar proportions of PWID had needles/syringes confiscated by the police in the last six months in both cities, but more PWID reported ever being incarcerated in Kohtla-Järve (55%) than in St. Petersburg (34%).

The majority of PWID in both cities had injected for more than 5 years with a mean age at first injection of just under 19 years (Table S.1). Past-month injection risk behaviours were lower in Kohtla-Järve and up to nine times less frequent than in St. Petersburg. Past-month polydrug use (injection of main and other drug) was equally widespread in both cities (47% and 41%). Fewer PWID in Kohtla-Järve had injected at least daily (24%) than in St. Petersburg (36%), shared needles and syringes (6% and 58%), filled from a used syringe (6% and 53%) or shared drug paraphernalia (7% and 68%).

Over three quarters of PWID in both cities had had sexual intercourse in the last 6 months and over half had a sex partner who injected drugs (55% in Kohtla-Järve and 58% in St. Petersburg). Over a third of PWID had multiple sex partners (34% and 49%) and 7% in Kohtla-Järve and 4% in St. Petersburg respectively had ever been paid for sex. Close to half of PWID always used condoms with casual partners in Kohtla-Järve (58%) and St. Petersburg (48%). Due to the high non-response rate (>50%) for some sexual risk behaviours in Kohtla-Järve, results for this city were not shown, given the high likelihood

of bias; we only analysed the effect of ATS- or opioid-injection for those variables in St. Petersburg (Table S.1). More than half of PWID tested positive for HIV in Kohtla-Järve (61%) and in St. Petersburg (56%). HCV and HSV reactivity measured in Kohtla-Järve only, was 75% and 32%, respectively.

Associations between primary ATS injection and injecting and sexual risk behaviours and serology in Kohtla-Järve

Determinants of ATS injection

Determinants of primary ATS injection are presented in Table 3. In Kohtla-Järve, ATS injectors were younger than opioid injectors with greater odds of being under 30 years of age (adjusted Odds Ratio (aOR) =2.1; 95%CI: 1.4-3.2) and of later injection initiation (aOR: 1.1; 95%CI: 1.0-1.4) than their opioid-injecting peers. The groups did not differ on other demographic characteristics. ATS injectors had lower odds of past-year drug treatment (aOR=0.5; 95%CI: 0.3-0.9), past-month contact with an NSP (aOR=0.2; 95%CI: 0.2-0.6), having needles/syringes confiscated by the police (aOR=0.3; 95%CI: 0.1-0.8) and incarceration (aOR=0.3; 95%CI: 0.2-0.5). They had higher odds of obtaining clean needles/syringes from a pharmacy than an NSP (aOR: 4.9 (95%CI: 3.5-6.9).

Associations with injecting risk behaviours

Primary ATS injection was associated with a number of injecting risk behaviours (Table 4). ATS injectors were more likely to have injected for less than 5 years (aOR=3.5; 95% CI: 1.9-6.2) (Table 4). ATS injection was negatively associated with frequent injecting (aOR=0.3; 95%CI: 0.2-0.6), lifetime needle/syringe-sharing (aOR= 0.3; 95%CI: 0.2-0.5) and back-loading (aOR= 0.4; 95%CI: 0.2-0.8) and was positively associated with polydrug use (aOR=2.0; 95%CI: 1.1-3.5). Past-month unsafe sharing practices such as sharing needles/syringe and drug paraphernalia were generally lower among primary ATS injectors but differences did not reach statistical significance (Table 4).

Associations with sexual risk behaviours

One third of PWID reported multiple sex partners with no significant difference between primary ATS- and opioid-injectors; however ATS injectors had greater odds of ever being paid for sex (aOR=2.6; 95%CI: 1.2-5.7)(Table 5).

Associations with HIV, HCV and HSV prevalence

Primary ATS injectors in Kohtla-Järve had lower odds of testing positive for HIV (aOR=0.6; 95%CI: 0.5-0.8) and having antibodies to HCV (aOR=0.5; 95%CI: 0.3-0.6) in

multivariate analysis, compared to primary opioid injectors (Table 6). HSV antibody status was not associated with ATS injection.

Associations between primary ATS injection and injecting and sexual risk behaviours and HIV in St. Petersburg

Determinants of ATS injection

In St. Petersburg, primary ATS injectors had higher odds of being under 30 years of age (aOR=6.8; 95%CI: 2.8-16.5), female (aOR=1.7; 95%CI: 0.7-4.1), of later initiation to injection (aOR: 1.3; 95%CI: 1.1-1.4) or having unstable living arrangements (aOR=2.2; 95%CI: 1.0-4.6) than opioid injectors (Table 3). Contact with NSP and drug treatment were very low in St. Petersburg and did not differ between ATS- and opioid-injectors. However ATS injectors had greater odds of obtaining needles and syringes from sources other than an NSP (e.g. from friends, other PWID, a drug dealer or in the street) (aOR=35; 95%CI: 2.7-472) and lower odds of having been incarcerated and having needles/syringes confiscated compared to opioid injectors.

Associations with injecting risk behaviours

Primary ATS injectors were more likely to report fewer than 5 years of injecting (aOR=8.3; 95%CI: 2.2-31.6)(Table 4). Several injecting risk behaviours were negatively associated with ATS injection. Primary ATS injectors had lower odds of daily or more frequent injecting (aOR=0.2; 95%CI: 0.1-0.9), injecting more than twice a day (aOR: 0.3; 95%CI: 0.1-0.6), sharing needles and syringes (aOR=0.2; 95%CI: 0.1-0.6), filling a syringe from a used syringe (aOR=0.2; 95%CI: 0.1-0.5) and sharing drug paraphernalia (aOR=0.3; 95%CI: 0.1-0.6) than opioid injectors. Polydrug use was frequent among both ATS- and opioid-injectors but did not differ significantly between the two groups.

Associations with sexual risk behaviours

Almost half of PWID in the Russian city reported multiple sex partners, with no significant difference between ATS- and opioid-injectors (Table 5). In multivariate analysis, ATS injectors had greater odds of being paid for sex (aOR=5.2; 95%CI: 1.0-27.0) and using condoms consistently with casual sex partners (aOR=8.0; 95%CI: 1.1-60.0).

Associations with HIV prevalence

Primary ATS injectors in St. Petersburg had lower odds of testing positive for HIV than PWID injecting opioid (aOR=0.3; 95%CI: 0.1-0.7)(Table 6). HCV and HSV serology were not collected in St. Petersburg.

DISCUSSION

We compared risk behaviours and HIV status among self-identified primary ATS-injectors and opioid-injectors in two settings with severe epidemics of drug use and HIV. Our results suggest that, in both locations, PWID primarily injecting ATS consistently differed on demographic characteristics and reported less or equally risky injecting behaviours compared to those who mainly injected opioids. ATS injectors in both cities were younger but started injecting later than opiate injectors, were more likely to report less than 5 years' injecting and generally at earlier stages in their drug injecting careers. The younger age and later onset of injecting among ATS injectors, suggested the emergence of a different group of PWID who may be at earlier stages of drug dependence and injecting less frequently than their opioid-injecting peers.

In St. Petersburg, contact with NSPs was generally low and did not differ between the two groups; there primary ATS injectors were less likely to have injected with used needles/syringes, shared drug paraphernalia or back-loaded than opiate injectors. However in Kohtla-Järve, where harm reduction services are established, ATS injectors were significantly less likely than opiate injectors to have had contact with NSPs and reported similar prevalence of sharing needles/syringes or drug paraphernalia. They were also less likely to back-load than opiate injectors. That more opiate injectors were in contact with NSPs (and OST) in Kohtla-Järve may have contributed to reducing risky injecting behaviours in this group, thus "levelling" injecting risk between the two drug groups.

Our findings are generally consistent with other studies, where self-reported primary ATS injection was associated with younger age and fewer years of injecting among PWID in Australia (Kaye, et al., 2000), the USA (Braine, et al., 2005), Canada (Fairbairn, et al., 2007), Ukraine and elsewhere in Estonia (Booth, et al., 2008; Talu, et al., 2010) and where primary ATS injectors reported similar or lower frequency of injection (Booth, et al., 2008; Braine, et al., 2005; Darke, et al., 2008; Gleghorn, et al., 1998; Kaye, et al., 2000; Maher, et al., 2007; Talu, et al., 2010) and similar frequency of needle and syringe-sharing than opiate injectors (Gleghorn, et al., 1998; Kaye, et al., 2000; Talu, et al., 2010). That primary ATS injectors in our study reported lower or similar injecting risk

behaviours than opiate injectors contrasts with findings from studies where ATS injection was not defined as main drug and occurred in the presence of other injection drugs, including heroin (Braine, et al., 2005; Crofts, et al., 1997; Hayashi, et al., 2011; Kozlov, et al., 2006; Martin, et al., 2010; Tavitian-Exley, et al., 2017). Injecting risk behaviours and infection risk associated with ATS injection may therefore differ depending on whether PWID inject ATS primarily or inject ATS in addition to or in combination with, addictive opiates such as heroin; these underline the need for consistent definitions and regular monitoring of drugs and drug combinations among PWID.

Both ATS-injectors and opioid-injectors in this study reported similarly high prevalence of sexual risk, including multiple sex partners. However primary ATS injectors were more likely to have ever been paid for sex. ATS may be used to increase energy, stamina, libido and to reduce social and sexual inhibition. Further, injection often occurs with peers or sexual partners, possibly generating more needle-sharing opportunities (Darke, et al., 1995; Klee, 1993). Several other studies of PWID also found positive associations between ATS injection and multiple sex partners, unprotected sex and trading sex for money or drugs (Lorvick, et al., 2006; Molitor, et al., 1999). The frequency of sexual risk in both cities and possible intersection with sex work highlight the potential for sexual transmission of HIV, and an unmet need to engage diverse PWID sub-groups with prevention and risk reduction messages emphasising sexual as well as injecting risks (Lorvick, et al., 2006; Molitor, et al., 1998; Rondinelli, et al., 2009).

Finally, HIV prevalence and HCV in Kohtla-Järve; were lower among ATS- than opioid-injectors, consistent with their shorter, cumulative exposure to risk resulting from younger age and later onset of injecting (Kozlov, et al., 2006; Martin, et al., 2010). These differences in HIV status remained after adjusting for factors such as injecting duration, suggesting that other determinants also play a role. Primary ATS injectors are nevertheless vulnerable to HIV acquisition as a result of their age (and gender in St. Petersburg), high prevalence of sexual risk behaviours and low contact with harm reduction services (i.e. NSP and drug substitution treatment in Kohtla-Järve).

The propensity of ATS injectors in Kohtla-Järve to obtain clean needles and syringes from pharmacies rather than NSPs when the majority of PWID in the sample were in contact with harm reduction services, also suggests they were not being reached (Vorobjov, et al., 2009). Furthermore, the lower odds of substitution treatment among ATS injectors in Kohtla-Järve may be expected since methadone-based substitution treatment has shown to reduce injecting risk behaviours and HIV infection and to support

adherence to highly active anti-retroviral therapy (HAART) among opioid users. However no proven pharmacological treatment exists for ATS-dependent injectors (Ahamad, et al., 2015; MacArthur, et al., 2012; World Health Organization, 2013). Where ATS use is prevalent, services that are tailored to the demographic characteristics and specific needs of ATS injectors and include psychosocial interventions, need to be integrated into harm reduction programmes (Mehrjerdi, et al., 2014; UNODC, 2010). The problem of ATS injection in these cities, and globally, requires effective low-threshold services able to engage injectors who are young and/or female, do not fit the drug use "profile" associated with heroin and neither seek nor desire contact with services focused on opioid injectors (Lorvick, et al., 2006; Pates, 2013; Shearer, et al., 2002; Vorobjov, et al., 2009).

Moreover, while few studies have looked at the life course of drug use among primary ATS injectors, especially in resource-limited settings (Brecht, et al., 2008), longitudinal and qualitative research would help to understand how primary ATS-injection and associated behavioural risks evolve over time. Consistent and systematic drug (and polydrug) monitoring would also contribute to better understanding heterogeneity among PWID.

Several limitations need to be acknowledged. First, our findings may only be generalizable to other PWID populations in Estonia or the Russian Federation. Second, obtaining standard probability samples of PWID populations is challenging, due to the hidden nature of this group, their stigmatised behaviours and the absence of a sampling frame. Although RDS surveys have demonstrated the ability to reach hidden population sub-groups, the representativeness of our samples cannot be verified (Abdul-Quader, et al., 2006; Heckathorn, 1997; Johnston, et al., 2010). Third, information on injecting and sexual risk behaviours was collected through self-reports and social desirability bias may affect the results. Self-reporting using interviewer-administered questionnaires has shown reliability in several studies and a 30-day period, as was used in this study, has shown to produce reliable recall on drug use and injecting behaviours among PWID (Darke, 1998; Des Jarlais, et al., 1999; Napper, et al., 2010). Additionally, the small number of ATS injectors in St. Petersburg resulted in wide confidence intervals that limited our analyses for this city. Finally, given the dynamic nature of drug use, high prevalence of polydrug use in this population and shorter recall, it is conceivable that misclassification may have occurred between ATS-and opioid-injectors thus leading to possible bias. However, non-differential misclassification of the exposure generally biased the inferences towards the null and, if this is the case here, our results could be considered conservative (Dosemeci, et al., 1990; Kirkwood, et al., 2003).

The strengths of this study include its large sample size and comparisons of two Eastern European locations reporting a high prevalence of HIV and injection of different drug classes. Recruitment of two large and diverse PWID samples was facilitated by the use of RDS and reported according to the STROBE-RDS statement (Johnston, et al., 2016; White, et al., 2015). We systematically compared PWID injecting different drug classes, using consistent definitions, study methods and tested tools and we highlighted important differences between self-identified primary ATS- and opioid-injectors that are of relevance to policy and programmes.

Primary ATS injectors reported lower or similar injecting risk behaviours, lower HIV prevalence and less engagement with services, than opioid injectors. Both groups had high levels of multiple sex partners but primary ATS injection was associated with paid sex, suggesting overlaps between injecting and sexual risk. Low threshold interventions (e.g. behavioural) and supplies targeting the needs of young stimulant injectors are needed to increase their contact with prevention services and reduce sexual risk behaviours. The coverage of harm reduction services, including sexual risk reduction, needs to be increased significantly in St. Petersburg for all PWID.

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Author contributions

RH, OL and AU designed the surveys in St. Petersburg and Kohtla-Järve and led surveys and data collection. ITE, MC and MMG developed the research idea and analysis plan, ITE conducted the statistical analyses and drafted the manuscript with MMG, MC and LP. RH, OL and AU provided critical review in the interpretation of results and manuscript. All authors reviewed the manuscript.

Declaration of interest: none declared

Table 1. HIV epidemic, context and response among people who inject drugs in Kohtla-Järve (Estonia) and St. Petersburg (Russia)

Indicator	Kohtla-Järve	St. Petersburg
HIV incidence	22 per 100 person-year *(2012)* (NIfHD, 2015; Uusküla, Des Jarlais, et al., 2015)	14.5 per 100 person-year *(2008)* (Niccolai, et al., 2011)
	All Estonia: 7.5 per 100 person-year *(2011)* (NIfHD, 2015; Uusküla, Des Jarlais, et al., 2015)	7.2per 100 person-year *(2010)* (Kozlov, et al., 2016)
HIV Prevalence	63% (95%CI: 56%-67%) (Uusküla, Raag, et al., 2015)	59% (95%CI: 52%-59%) (Uusküla, Raag, et al., 2015)
PWID population size estimate	2,000 (range: 700-2,500) All Estonia: 5,362 (range: 3,906–9,837) (Uusküla, et al., 2013)	83,120 (95%CI:77,320 -88,920) (Heimer, et al., 2010)
% of population who inject drugs	4.5% *(2012)* (Wu J, et al., under review)	5.5% *(2008)* (Heimer, et al., 2010)
Needle/syringe services (start year)	2004	1996
Needle/syringe services (n, type)	5 outreach, 3 fixed NSP (NIfHD, 2016)	2 mobile, 2 fixed site services *(2015)*
Clean syringes per PWID per year	All Estonia: 125 syringes/PWID per year *(2011)*	n/a
Needle/syringes services provided by	NGOs	City AIDS centre (as of 2015), NGOs
Drug substitution (start year)	2004	OST illegal
Type of drug treatment	Opiate substitution	Detoxification only (21 days)
Coverage (%, n and year)	All Estonia: 15% of PWID (n=919, *2014*)(NIfHD, 2016)	11% PWID registered, % in treatment n/a
Drug treatment services provided by	NGOs, clinics	Centralized, in-patient

Table 1: Reference population for Estonia aged 15-44 years old; for St Petersburg aged 20-45 years old. Data collection years are italicised. HIV= Human Immune deficiency virus. PWID people who inject drugs. CI=Confidence Interval. NSP= Needle and Syringe Programme. OST=Opiate Substitution treatment. NGO= Non-governmental organisation. N/a=not available.

Table 2. Characteristics of sample and by reported primary amphetamine injection in Kohtla-Järve (Estonia) **and St. Petersburg** (Russian Federation)

	Kohtla-Järve				St. Petersburg			
CHARACTERISTICS	**All[(1)] PWID Kohtla-Järve**	N	**Primary amphetamine (%)[(1)]**	n	**All[(1)] PWID St. Petersburg**	N	**Primary amphetamine (%)[(1)]**	n
DEMOGRAPHIC VARIABLES		591		195		811		27
Sex								
Female	**26%**	155	29.7%	58	**22%**	180	48.2%	13
Male	**74%**	434	70.3%	137	**78%**	631	51.9%	14
Missing		2		0		0		0
Age group								
< 30 years	**50%**	294	61.5%*	120	**30%**	241	74.1%*	20
>= 30 years	**50%**	297	38.5%	75	**70%**	570	25.9%	7
Missing		0		0		0		0
Ethnicity								
Estonian	**12%**	66	12.3%	24	**0%**	0	0%	0
Other	**7%**	43	5.1%	10	**4%**	36	3.7%	1
Russian	**81%**	481	82.6%	161	**96%**	775	96.3%	26
Missing		1		0		0		0
Education completed								
Basic (9th grade)/vocational	**80%**	472	81.0%	158	**58%**	475	29.6%*	8
Secondary (11th grade)	**19%**	116	19.0%	37	**30%**	243	51.9%	14
Higher *(St. Petersburg only)*	**1%**	3	0%	0	**12%**	93	18.5%	5
Missing		0		0		0		0
Living arrangements								
Unstable (hostel, dormitory, shelter)	**40%**	238	39.5%	77	**36%**	292	51.9%*	14
Stable (own or partner's flat/house)	**60%**	352	60.5%	118	**64%**	519	48.2%	13
Missing		1		0		0		0
Main income source								
irregular/illicit (SP only)	**3%**	15	-	-	**16%**	134	3.7%	1
non-regular/dependant	**33%**	193	38.5%	74	**39%**	312	37.0%	10
regular/salaried	**64%**	375	61.5%	118	**45%**	362	59.3%	16
Missing		8		3		3		0
CONTEXTUAL VARIABLES								
Lifetime drug treatment								
Ever had drug treatment	**55%**	324	32.8%*	64	**72%**	582	25.9%*	7
Never in treatment	**45%**	267	67.2%	131	**28%**	229	74.1%	20
Missing		0		0		0		0
Drug/substitution treatment								
Yes (12 months)	**13%**	75	6.7%*	13	**11%**	86	14.8%	4
No	**87%**	516	93.3%	182	**89%**	724	85.2%	23
Missing		0		0		1		0
NSP programme *(4 weeks)*								
Contact with NSP	**82%**	451	66.7%*	124	**16%**	119	3.7%*	1
No contact with NSP	**18%**	102	33.3%	62	**84%**	645	96.3%	26
Missing		38		9		47		0
Source of clean needle/syringes								
Other (friend, dealer, street)	**5%**	27	66.7%*	124	**4%**	30	40.7%*	11
Pharmacist/chemist	**13%**	75	26.3%	49	**81%**	615	55.6%	15
NSP	**82%**	451	7.0%	13	**16%**	119	3.7%	1
Missing		38		9		47		0
Incarceration								
Ever in prison	**55%**	324	30.3%*	59	**34%**	274	7.4%*	2
Never in prison	**45%**	267	69.7%	136	**66%**	537	92.6%	25
Missing		0		0		0		0
Needles/syringes confiscated								
Had N/S confiscated	**31%**	404	15.9%*	31	**26%**	212	0%	0
No N/S confiscated	**69%**	184	84.1%	164	**74%**	599	100%	27
Missing		3		0		0		0

Table 2: (1) Column percentage. Crude estimates are presented for Kohtla-Järve and St. Petersburg; adjusted estimates using respondent driven sampling weights (RDS-II, Volz-Heckathorn) are shown in supplementary material as is the number of missing observations. NSP=Needle and syringe programme. HIV= Human Immune deficiency Virus. (2) Drug/substitution treatment in last 12 months refers to opiate drug substitution (OST) in Kohtla-Järve and to detoxification (non-OST) in St Petersburg. *Statistically significant result in comparisons of ATS- and opioid-injectors using Pearson's Chi-squared test for proportions (p-value <0.05) or Fisher's exact when expected cell count is <4.

Table 3. Predictors of primary ATS injection in Kohtla-Järve (Estonia) **and St. Petersburg** (Russian Federation)

DEMOGRAPHIC CHARACTERISTICS *(reference: opioid injectors)*	**Kohtla-Järve - ATS** injectors (n=195) **OR**[(1)]**95% CI**	**aOR**[(2)]**95%CI**	**St. Petersburg - ATS** injectors (n=27) **OR**[(1)]**95% CI**	**aOR**[(2)]**95%CI**
Sex				
Female	1.3(0.9-1.9)	1.3 (0.9-1.6)	3.4 (1.0-11.5)	1.7 (0.7- 4.1)
Male	*ref*	*ref*	*ref*	*ref*
Age group				
< 30 years	**2.0 (1.3-3.3)**	**2.1 (1.4-3.2)**	**7.3 (2.6-20.3)**	**6.8 (2.8-16.5)**
>= 30 years	*ref*	*ref*	*ref*	*ref*
Ethnicity				
Estonian	1.2 (0.8-1.9)	1.1 (0.6-2.1)	-	-
Other	0.6 (0.2-1.8)	0.6 (0.3-1.1)	0.8 (0.1-9.2)	0.8 (0.1-11.4)
Russian	*ref*		*ref.*	*ref.*
Education completed				
Basic (9th grade)/vocational	1.1 (0.6-1.8)	1.0 (0.6-1.7)	0.3 (0.05-1.7)	**2.6 (1.2-6.7)**
Secondary (11th grade)	*ref*	*ref*	1.1 (0.4-3.2)	2.5 (0.7-9.6)
Higher *(St. Petersburg only)*	-	-	*ref*	*ref*
Living arrangements				
Unstable (hostel, dorm, shelter)	0.9 (0.6-1.4)	0.9 (0.6-1.2)	2.0 (0.9-4.1)	**2.2 (1.0-4.6)**
Stable (own/partner home)	*ref*	*ref*	*ref*	*ref*
Main income source				
irregular/illicit *(SP only)*	-	-	0.2 (0.02-1.6)	0.1 (0.05-1.5)
non-regular/dependant	1.3 (0.9 -1.7)	1.0 (0.6 -1.5)	0.7 (0.4-1.5)	0.8 (0.4-1.5)
regular/salaried	*ref.*	*ref.*	*ref*	*ref*
Age at first injection				
Primary ATS/Opioid	**1.1 (1.1-1.2)**	**1.1 (1.0-1.2)**	**1.1 (1.0-1.3)**	**1.3 (1.1-1.4)**
CONTEXTUAL VARIABLES				
Lifetime drug treatment				
Ever drug treatment	**0.2 (0.2-0.3)**	**0.3 (0.2-0.5)**	**0.2 (0.1-0.6)**	**0.2 (0.1-0.5)**
Never in treatment	*ref*	*ref*	*ref*	*ref*
Drug/substitution treatment				
Yes *(12 months)*	**0.4(0.2-0.7)**	**0.5 (0.3-0.9)**	1.5 (0.4-5.8)	1.9 (0.3-12.7)
No	*ref.*	*ref*	*ref*	*ref*
NSP programme *(4 weeks)*				
Contact with NSP	**0.2 (0.1-0.3)**	**0.2 (0.2-0.6)**	0.2 (0.05-1.0)	**0.4 (0.1-2.2)**
No contact with NSP	*ref*	*ref*	*ref*	*ref*
Source of clean needle/syringes				
Other (friend, dealer, street)	2.4 (0.7-9.9)	2.0 (0.5-7.9)	**67 (8.1-544)**	**35 (2.7-472)**
Pharmacist/chemist	**6.0 (4.1-8.6)**	**4.9 (3.5-6.9)**	2.9 (0.6-14.2)	1.8 (0.3-9.3)
NSP	*ref*	*ref*	*ref*	*ref*
Incarceration				
Ever in prison	**0.2 (0.1-0.3)**	**0.3 (0.2-0.5)**	**0.2 (0.1-0.3)**	**0.2 (0.1-0.8)**
Never in prison	*ref*	*ref*	*ref*	*ref*
Needles/syringes confiscated				
Had N/S confiscated	**0.3 (0.1-0.9)**	**0.3 (0.1-0.8)**	-	*Too few obs.*
No N/S confiscated	*ref*	*ref*		

Table 3. (1) Odds ratio (OR) with 95% confidence intervals (95% CI) refer to primary Amphetamine-Type Stimulant (ATS) versus opioids (reference group is "primary opioid injectors"). (2) Multivariable model for ATS was adjusted for predictors: age, sex, education, duration of injecting (and living arrangements in St. Petersburg). Statistically significant results at the $\alpha < 0.05$ are marked in bold. (3) Needle/syringe programme (NSP), drug treatment and needles/syringes confiscated were adjusted for in models where the outcome was injecting risk. (4) Drug/substitution treatment in last 12 months refers to opiate drug substitution (OST) in Kohtla-Järve and to detoxification (non-OST) in St Petersburg.

Table 4. Association between ATS injection and injecting risk behaviours (Kohtla-Järve, St. Petersburg)

OUTCOMES: INJECTING RISK *(3)*	**Kohtla-Järve – ATS** injectors (n=195)		**St. Petersburg – ATS** injectors (n=27)	
(reference: opioid injectors)	**OR(1)95% CI**	**aOR(2)95%CI**	**OR(1)95% CI**	**aOR(2)95%CI**
Duration of injecting				
≤ 5 years	**6.1 (3.8-9.6)**	**3.5 (1.9-6.2)**	**14.7 (4.2-51)**	**8.3 (2.2-31.6)**
> 5 years	*ref.*	***ref***	*ref.*	***ref***
Frequency of injecting				
Daily or more	**0.2 (0.1-0.5)**	**0.3 (0.2-0.6)**	0.2 (0.1-1.0)	**0.2 (0.1-0.9)**
Less than daily	*ref.*	*ref.*	*ref.*	***ref.***
Ever shared needles/syringes				
Yes	**0.2 (0.1-0.3)**	**0.3 (0.2-0.5)**	**0.05 (0.03-0.1)**	**0.1 (0.1-0.2)**
No	*ref.*	***ref.***	*ref.*	***ref.***
Injected w/used needles/syringes				
Yes	0.5 (0.1-1.6)	0.5 (0.2-1.5)	**0.1 (0.05-0.3)**	**0.2 (0.1-0.6)**
No	*ref.*	*ref.*	*ref.*	***ref.***
Filled from working syringe (back-loaded)				
Yes	0.4 (0.2-1.2)	**0.4 (0.2-0.8)**	**0.1 (0.1-0.3)**	**0.2 (0.1-0.5)**
No	*ref.*	***ref.***	*ref.*	***ref.***
Shared drug paraphernalia				
Yes	0.5 (0.2-1.3)	0.5 (0.3-1.2)	**0.2 (0.1-0.3)**	**0.3 (0.1-0.6)**
No	*ref.*	*ref.*	*ref.*	***ref.***
Any polydrug use *(any)*				
≥ 2 drugs	**2.2 (1.5-3.4)**	**2.0 (1.1-3.5)**	0.7 (0.4-1.2)	0.7 (0.4-1.2)
Main drug only	*ref.*	*ref.*	ref.	ref.

Table 4. (1) Odds ratio (OR) with 95% confidence intervals (95% CI) refer to primary Amphetamine-Type Stimulant (ATS) versus opioids (reference group). (2) Multivariable models were adjusted for age, sex, education, duration of injecting, needle/syringe programme (NSP), drug/substitution treatment, needles/syringes (N/S) confiscated (and living arrangements in St. Petersburg). Statistically significant results at the $\alpha < 0.05$ are marked in bold. (3) Injecting risk in the last 4 weeks.

Table 5. Associations between ATS injection and sexual risk behaviours (Kohtla-Järve, St. Petersburg)

OUTCOMES: SEXUAL RISK *(3)*	**Kohtla-Järve - ATS** injectors (n=195)		**St. Petersburg - ATS** injectors (n=27)	
(reference: opioid injectors)	**OR(1)95% CI**	**aOR(2)95%CI**	**OR(1)95% CI**	**aOR(2)95%CI**
Any sex in 6 months				
Yes	1.8 (1.0-3.3)	1.7 (0.9-3.3)	1.8 (0.8-3.9)	1.6 (0.7- 3.8)
No	*ref.*	*ref*	*ref.*	*ref*
Regular sex partner injects				
Yes	0.7 (0.4-1.1)	0.8 (0.5-1.9)	0.8 (0.2-3.3)	0.8 (0.2- 3.0)
No	*ref.*	*ref*	*ref.*	*ref*
Casual sex partner injects				
Yes	1.1 (0.8-1.5)	1.8 (0.5-7.1)	0.5 (0.1-2.6)	0.4 (0.1-2.2)
No	*ref.*	*ref*	ref.	ref
Was ever paid for sex				
Yes	1.3 (0.9-1.8)	**2.6 (1.2-5.7)**	**12.2 (3.7-40)**	**5.2 (1.0-27)**
No	*ref.*	*ref*	*ref.*	*ref*
Multiple sex partners				
>= 2 sex partners	0.8 (0.4-1.6)	0.7 (0.3-1.5)	0.9 (0.5-1.8)	0.7 (0.3-1.6)
one sex partner	*Ref*	*ref*	*ref*	*ref*
Condom with regular partner				
Yes (consistent)	0.9 (0.7-1.4)	1.0 (0.7-1.4)	1.9 (0.4-4.6)	1.5 (0.5-4.5)
No	*ref.*	*ref*	*ref*	*ref*
Condom with casual partner				
Yes (consistent)	1.4 (0.6-3.0)	1.2 (0.6-2.6)	**10.4 (1.9-57)**	**8.0 (1.1-60)**
No	*ref.*	*ref*	*ref*	*ref*

Table 5:(1) Odds ratio (OR) with 95% confidence intervals (95% CI) refer to primary Amphetamine-Type Stimulant (ATS) versus opioids (reference group). (2) Multivariable models were adjusted for age, sex, education, duration of injecting, needle/syringe programme (NSP), drug /substitution treatment, needles/syringes (N/S) confiscated (and living arrangements in St. Petersburg). Statistically significant results at the $\alpha < 0.05$ are marked in bold. (3) Sexual risk in the last 6 months.

Table 6. Associations between ATS injection and serological markers (Kohtla-Järve, St. Petersburg)

SEROLOGICAL MARKERS *(3)*	**Kohtla-Järve - ATS** injectors (n=195)		**St. Petersburg - ATS** injectors (n=27)	
(reference: opioid injectors)	**OR[(1)]95% CI**	**aOR[(2)]95%CI**	**OR[(1)]95% CI**	**aOR[(2)]95%CI**
HIV status				
Positive	**0.4 (0.3-0.6)**	**0.6 (0.5-0.8)**	**0.2 (0.1-0.4)**	**0.3 (0.1-0.7)**
Negative	*ref*	***ref***	*ref*	***ref***
Hepatitis C				
HCV reactive	**0.3 (0.2-0.4)**	**0.5 (0.3-0.6)**	Not collected	Not collected
Non-reactive	*ref.*	***ref***	-	-
HSV-2 status				
Positive	1.0 (0.6-1.6)	1.2 (0.7-2.0)	Not collected	Not collected
Negative	*ref.*	*ref*	-	**-**

Table 6: (1) Odds ratio (OR) with 95% confidence intervals (95% CI) refer to primary Amphetamine-Type Stimulant (ATS) versus opioids (reference group). (2) Multivariable models were adjusted for age, sex, education, duration of injecting, needle/syringe programme (NSP), drug /substitution treatment, needles/syringes (N/S) confiscated (and living arrangements in St. Petersburg). Statistically significant results at the $\alpha < 0.05$ are marked in bold. HIV= Human Immune deficiency Virus. HCV=Hepatitis C and HSV-2=Herpes Simplex Virus.

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